(FILE 'HOME' ENTERED AT 10:44:22 ON 04 APR 2006)

FILE 'CAPLUS, MEDLINE' ENTERED AT 10:44:34 ON 04 APR 2006

L1	20540	S	INFLAMM? AND (NITRIC (W) OXIDE)
L2	7523	S	L1 AND (TREATMENT OR MANAGEMENT OR PROTOCOL OR THERAPY)
L3	0	S	L2 AND (EXHALATION(W)RATE)
L4	5	S	L2 AND (EXHALATION(5A)RATE)
L5	220	S	L1 AND ((NITRIC(W)OXIDE)(5A)(CONCENTRATION OR PPB))
L6	0	S	L5 AND (DOSAGE (5A) (CHANGE? OR ADJUST?))
L7	11	S	L5 AND BASELINE

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
TI Exhaled **nitric oxide** in asthmatics and healthy volunteers
AB The effects of asthmatic airway **inflammation** and **exhalation** flow **rate** on exhaled **nitric oxide** (NO) concentration were studied. The repeatability of the test and normal day-to-day variation of exhaled NO in healthy volunteers were also evaluated during a two-week period. The study involved 13 diagnosed asthmatic men who had not yet started **treatment** with anti-**inflammatory** glucocorticoids and 10 healthy volunteers who performed exhaled NO measurements using different exhalation flow rates. The asthmatic men had significantly higher NO concentration in their exhaled air compared to healthy volunteers. The **exhalation** flow **rate** had a major effect on exhaled NO in both asthmatic and healthy volunteers. No levels in exhaled air seemed to be a neg. exponential function and NO excretion was a pos. linear function of **exhalation** flow **rate**. This showed that exhaled NO could be used to monitor airway **inflammation**.
ACCESSION NUMBER: 2001:597391 CAPLUS
DOCUMENT NUMBER: 136:277142
TITLE: Exhaled **nitric oxide** in asthmatics and healthy volunteers
AUTHOR(S): Lehtimaki, Lauri; Saarelainen, Seppo; Kankaanranta, Hannu; Turjanmaa, Vaino; Moilanen, Eeva
CORPORATE SOURCE: The Immunopharmacological Research Group, Medical School, University of Tampere, Tampere, FIN-33101, Finland
SOURCE: Portland Press Proceedings (2000), 16(Biology of Nitric Oxide, Part 7), 91
CODEN: POPPEF; ISSN: 0966-4068
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 5 MEDLINE on STN
TI NO in exhaled air of asthmatic children is reduced by the leukotriene receptor antagonist montelukast.
AB **Nitric oxide** in exhaled air (FENO) is increased in asthmatic children, probably reflecting aspects of airway **inflammation**. We have studied the effect of the leukotriene receptor antagonist (LTRA) montelukast on FENO with a view to elucidate potential anti-**inflammatory** properties of LTRAs. Twenty-six asthmatic children 6 to 15 yr of age completed a double-blind crossover trial of 2 wk of **treatment** with 5 mg montelukast once daily versus placebo. FENO was measured during single-breath **exhalation** at a constant flow **rate** of 0.1 to 0.13 L/s against a resistance of 10 kPa/L/s. Eleven children were receiving maintenance **treatment** with inhaled steroids during the study (mean daily dose, 273 microgram), whereas the other 15 used only inhaled beta(2)-agonists as required. The within-subject coefficient of variation of FENO over a 2-wk interval for the 26 children was 38%. FENO was significantly reduced by 20% after the 2-wk **treatment** with montelukast as compared with placebo as well as compared with baseline. This effect occurred rapidly with a 15% fall in FENO within 2 d. The effect of montelukast on FENO was independent of concurrent steroid **treatment**. The effect on FENO is probably not caused by bronchodilatation since FENO increased significantly after inhalation of terbutaline. In conclusion, FENO in asthmatic children was significantly decreased from montelukast, which corroborates anti- **inflammatory** properties of LTRA.
ACCESSION NUMBER: 1999439836 MEDLINE

DOCUMENT NUMBER:	PubMed ID: 10508811
TITLE:	NO in exhaled air of asthmatic children is reduced by the leukotriene receptor antagonist montelukast.
AUTHOR:	Bisgaard H; Loland L; Oj J A
CORPORATE SOURCE:	Department of Paediatrics, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark.. Bisgaard@RH.DK
SOURCE:	American journal of respiratory and critical care medicine, (1999 Oct) Vol. 160, No. 4, pp. 1227-31. Journal code: 9421642. ISSN: 1073-449X.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	(CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE:	English
FILE SEGMENT:	Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:	199911
ENTRY DATE:	Entered STN: 20000111 Last Updated on STN: 20000111 Entered Medline: 19991116

ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Dose-response relationship and reproducibility of the fall in exhaled **nitric oxide** after inhaled beclomethasone dipropionate therapy in asthma patients

AB The fractional **concn.** of exhaled **nitric oxide** (FENO) is a marker of asthmatic airway **inflammation**. We determined the dose response and the reproducibility of the FENO fall following inhaled beclomethasone dipropionate (iBDP) therapy in nonsteroid-treated asthmatic patients. Study A: For four 1-wk periods (period 1 to period 4), the following regimens were administered in sequential order to 15 nonsteroid-treated asthmatic patients: period 1, placebo; period 2, 100 μg/d of iBDP; period 3, 400 μg/D of iBDP; and period 4, 800 μg/d of iBDP. Spirometry, FENO, and provocative concentration of methacholine resulting in a 20% fall in FEV1 (PC20) were measured at each of five visits (visit 1 to visit 5). Study B: During four periods, 12 nonsteroid-treated asthmatic patients received placebo treatment for 7 days (period 1), 200 μg/d of iBDP for 14 days (period 2), washout on placebo treatment until the FENO was within 15% of **baseline** (period 3), and 200 μg/d of iBDP for 14 days (period 4). Study A: Mean FEV1 rose progressively from 3.10 L (visit 1) to 3.41 L (visit 5; $p = 0.001$). All iBDP doses caused a significant FEV1 rise compared to placebo treatment, but with no significant separation of doses using FEV1. FENO geometric mean (95% confidence limits) fell progressively from 103.5 ppb (ppb) (78.5 to 136.7) to 37.4 ppb (29.1 to 48.0) from visit 1 to visit 5 ($p = 0.001$). All doses of iBDP resulted in a significant change in FENO from placebo treatment, but with significant separation of only the 100-μg and 800-μg doses by FENO. Geometric mean (95% confidence limits) PC20 rose progressively from 0.01 mg/mL (0.00 to 0.19) to 0.48 mg/mL (0.01 to 8.1) from visit 1 to visit 5 ($p = 0.002$). All doses of iBDP resulted in a significant change in PC20 from **baseline** or placebo treatment, but with no significant separation of active iBDP doses using PC20. Study B: FENO fell from 111.56 ppb (80.3 to 155.1) to 66.3 ppb (49.2 to 89.5; $p < 0.001$) from period 1 to period 2, and from 110.2 ppb (79.3 to 153.1) to 61.7 ppb (42.9 to 88.8; $p < 0.001$) from period 3 to period 4. There were no significant differences between FENO in period 1 and period 3 ($p = 0.83$) or between period 2 and period 4 ($p = 0.220$). FENO was superior to FEV1 and PC20 in separating doses of iBDP. The fall in FENO after two identical administrations of iBDP separated by placebo washout was highly reproducible.

ACCESSION NUMBER:	2001:433779 CAPLUS
DOCUMENT NUMBER:	135:266968
TITLE:	Dose-response relationship and reproducibility of the fall in exhaled **nitric oxide** after inhaled beclomethasone dipropionate therapy in asthma patients
AUTHOR(S):	Silkoff, Philip E.; McClean, Patricia; Spino, Michael; Erlich, LuAnn; Slutsky, Arthur S.; Zamel, Noe
CORPORATE SOURCE:	Toronto Hospital, Toronto, ON, Can.
SOURCE:	Chest (2001), 119(5), 1322-1328 CODEN: CHETBF; ISSN: 0012-3692
PUBLISHER:	American College of Chest Physicians
DOCUMENT TYPE:	Journal
LANGUAGE:	English
REFERENCE COUNT:	17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 11 MEDLINE on STN

TI Exhaled **nitric oxide** in children with asthma receiving Xolair (omalizumab), a monoclonal anti-immunoglobulin E antibody.

AB OBJECTIVE: To evaluate the effect of a humanized monoclonal antibody to immunoglobulin E, omalizumab (Xolair, Novartis Pharmaceuticals, East Hanover, NJ; Genentech Inc, South San Francisco, CA), on airway **inflammation** in asthma, as indicated by the fractional **concentration** of exhaled **nitric oxide**

(FE(NO)), a noninvasive marker of airway **inflammation**. Xolair was approved recently by the US Food and Drug Administration for moderate-to-severe allergic asthma in adolescents and adults. STUDY DESIGN: As an addendum at 2 sites to a randomized, multicenter double-blind, placebo-controlled trial, FE(NO) was assessed in children with allergic asthma over 1 year. There were 3 consecutive study periods: 1) stable dosing of inhaled beclomethasone dipropionate (BDP) when the dose was optimized (period of 16 weeks); 2) inhaled steroid-reduction phase (period of 12 weeks), during which BDP was tapered if subjects remained stable; and 3) open-label extension phase, during which subjects receiving placebo were switched to active omalizumab (period of 24 weeks). The primary outcome was area under the FE(NO) versus time curve (AUC) for adjusted FE(NO), defined as the ratio of FE(NO) at each time point compared with the value at **baseline**. RESULTS: Twenty-nine subjects participated and were randomized to omalizumab (n = 18) and placebo (n = 11) treatment groups in a 2:1 ratio dictated by the main study. There was a significant difference for age, resulting in a difference in absolute forced expiratory volume in 1 second but no difference in asthma severity based on the forced expiratory volume in 1 second percentage predicted. **Baseline** BDP dose was comparable between groups, as were **baseline** values of mean FE(NO) (active: 38.6 +/- 25.6 ppb; placebo: 52.7 +/- 52.9 ppb). The degree of BDP dose reduction during the steroid-reduction and open-label phases was equivalent between the omalizumab and placebo-treated groups; subjects in the omalizumab- and placebo-treated groups had reduced their BDP dose by an average of 51% and 60%, respectively, at the end of the steroid-reduction phase and by 68% and 94%, respectively, by the end of the open-label period. In the active and placebo groups, 44% and 27% and 75% and 73% of subjects had stopped use of inhaled corticosteroids at the end of the steroid-reduction and open-label phases, respectively. There was no significant difference between the active and placebo groups during the steroid-stable phase for AUC of adjusted **nitric oxide** (1.31 +/- 1.511 vs 1.45 +/- 0.736). However, during the steroid-reduction phase, the variability of adjusted FE(NO) in the placebo-treated group was greater than that of the omalizumab-treated group at most visits, with a significant difference between groups for AUC of adjusted **nitric oxide** (0.88 +/- 0.69 vs 1.65 +/- 1.06). FE(NO) fell from 82.1 +/- 55.6 ppm at the end of the steroid-reduction phase to 33.3 +/- 21.6 ppb at the end of the open-label period in the placebo group who were placed on active omalizumab. This decrease occurred while the mean dose of BDP remained very low. Analysis of FE(NO) over 52 weeks of omalizumab treatment in the active group demonstrated that there was a significant reduction from **baseline** to the end of the open-label period (41.9 +/- 29.0 to 18.0 +/- 21.8 ppb) despite a high degree of steroid reduction. CONCLUSION: In this preliminary study based on FE(NO), a noninvasive marker of airway **inflammation**, treatment with omalizumab may inhibit airway **inflammation** during steroid reduction in children with allergic asthma. The degree of inhibition of FE(NO) was similar to that seen for inhaled corticosteroids alone, suggesting an antiinflammatory action for this novel therapeutic agent in asthma. This is in keeping with recent evidence that omalizumab inhibits eosinophilic **inflammation** in induced sputum and endobronchial tissue.

ACCESSION NUMBER: 2004167212 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15060258
TITLE: Exhaled **nitric oxide** in children with asthma receiving Xolair (omalizumab), a monoclonal anti-immunoglobulin E antibody.
AUTHOR: Silkoff Philip E; Romero Francisco A; Gupta Niroo; Townley Robert G; Milgrom Henry
CORPORATE SOURCE: Department of Medicine, National Jewish Medical and Research Center and the University of Colorado Health Sciences Center, Denver, Colorado 80206, USA.. philsilkoff@hotmail.com

SOURCE: Pediatrics, (2004 Apr) Vol. 113, No. 4, pp. e308-12.
Journal code: 0376422. E-ISSN: 1098-4275.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040406
Last Updated on STN: 20040514
Entered Medline: 20040513

ANSWER 9 OF 11 MEDLINE on STN

TI Dose-response relationship and reproducibility of the fall in exhaled **nitric oxide** after inhaled beclomethasone dipropionate therapy in asthma patients.

AB STUDY OBJECTIVES: The fractional **concentration** of exhaled **nitric oxide** (FENO) is a marker of asthmatic airway **inflammation**. We determined the dose response and the reproducibility of the FENO fall following inhaled beclomethasone dipropionate (iBDP) therapy in nonsteroid-treated asthmatic patients. STUDY DESIGN: Study A: For four 1-week periods (period 1 to period 4), the following regimens were administered in sequential order to 15 nonsteroid-treated asthmatic patients: period 1, placebo; period 2, 100 microg/d of iBDP; period 3, 400 microg/D of iBDP; and period 4, 800 microg/d of iBDP. Spirometry, FENO, and provocative concentration of methacholine resulting in a 20% fall in FEV(1) (PC(20)) were measured at each of five visits (visit 1 to visit 5). Study B: During four periods, 12 nonsteroid-treated asthmatic patients received placebo treatment for 7 days (period 1), 200 microg/d of iBDP for 14 days (period 2), washout on placebo treatment until the FENO was within 15% of **baseline** (period 3), and 200 microg/d of iBDP for 14 days (period 4). RESULTS: Study A: Mean FEV(1) rose progressively from 3.10 L (visit 1) to 3.41 L (visit 5; p = 0.001). All iBDP doses caused a significant FEV(1) rise compared to placebo treatment, but with no significant separation of doses using FEV(1). FENO geometric mean (95% confidence limits) fell progressively from 103.5 parts per billion (ppb) (78.5 to 136.7) to 37.4 ppb (29.1 to 48.0) from visit 1 to visit 5 (p = 0.001). All doses of iBDP resulted in a significant change in FENO from placebo treatment, but with significant separation of only the 100-microg and 800-microg doses by FENO. Geometric mean (95% confidence limits) PC(20) rose progressively from 0.01 mg/mL (0.00 to 0.19) to 0.48 mg/mL (0.01 to 8.1) from visit 1 to visit 5 (p = 0.002). All doses of iBDP resulted in a significant change in PC(20) from **baseline** or placebo treatment, but with no significant separation of active iBDP doses using PC(20). Study B: FENO fell from 111.56 ppb (80.3 to 155.1) to 66.3 ppb (49.2 to 89.5; p < 0.001) from period 1 to period 2, and from 110.2 ppb (79.3 to 153.1) to 61.7 ppb (42.9 to 88.8; p < 0.001) from period 3 to period 4. There were no significant differences between FENO in period 1 and period 3 (p = 0.83) or between period 2 and period 4 (p = 0.220). CONCLUSIONS: FENO was superior to FEV(1) and PC(20) in separating doses of iBDP. The fall in FENO after two identical administrations of iBDP separated by placebo washout was highly reproducible.

ACCESSION NUMBER: 2001410544 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11348935
TITLE: Dose-response relationship and reproducibility of the fall in exhaled **nitric oxide** after inhaled beclomethasone dipropionate therapy in asthma patients.
AUTHOR: Silkoff P E; McClean P; Spino M; Erlich L; Slutsky A S; Zamel N
CORPORATE SOURCE: Toronto Hospital, Toronto, Ontario, Canada.. silkoffp@njc.org
SOURCE: Chest, (2001 May) Vol. 119, No. 5, pp. 1322-8. Journal code: 0231335. ISSN: 0012-3692.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723 Last Updated on STN: 20020911 Entered Medline: 20010719